REMARKS

Claim 1, as amended, and claims 3, 7, 17, 19, and 22 are pending in the instant application. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

1. Rejection of claims 1 and 17 under 35 U.S.C. § 102

The Office Action asserts a rejection of claims 1 and 17 under 35 U.S.C. § 102(b), as being anticipated by International Publication No. WO 95/22626 (Meijer *et al.*). The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a mixture of probes that is specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58, but not specific for a variety of low-risk HPV types. The Action also states that because there would be more than one copy of each of the individual oligonucleotide probes in the reagent disclosed by Meijer *et al.*, the copies of each oligonucleotide probe comprise "a plurality of nucleic acid fragments." The Action also states that the copies of each oligonucleotide probe are "fragments of the full-length genomic sequence." The Action therefore concludes that the reagent disclosed by Meijer *et al.* is considered to include a plurality of genomic HPV DNA probes sets, wherein the individual genomic probe sets comprise a plurality of nucleic acid fragments of essentially the full-length genomic sequence of HPV types 16, 18, 31, 33, 35, or 51. The Action also states that the probe cocktail disclosed by Meijer *et al.* would have inherently been in a container.

Applicants respectfully disagree with the Action's assertion that the reagent recited in claim 1 encompasses the oligonucleotide cocktail disclosed by Meijer *et al.* As discussed in Applicants' response to the Office Action mailed June 26, 2003, and again in Applicants' response to the Office Action mailed January 22, 2004, Meijer *et al.* disclose *oligonucleotide* primers of only 23-28 nucleotides for amplifying HPV DNA present in a sample by polymerase chain reaction, and *oligonucleotide* probes of only 30 nucleotides for HPV genotyping of the amplification product. The reagent of claim 1, on the other hand, comprises "a plurality of *genomic* HPV DNA probes sets" (*emphasis added*). In addition, the instant specification teaches that the reagent of the invention

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comprises genomic HPV DNA probes that "are *not* similar to oligonucleotide probes as used in the prior art" (page 5, paragraph 1) (*emphasis added*). Moreover, the difference between the genomic probes recited in claim 1 and the oligonucleotide probes disclosed by Meijer *et al.* is well understood in the art. Specifically, one of ordinary skill in the art would understand that the oligonucleotide probes disclosed by Meijer *et al.* correspond to a small portion of the entire HCV genome (about 0.38%), while genomic probes comprise a plurality of nucleic acid fragments that detectably hybridize to essentially the full-length genomic sequence. In addition, Faulkner-Jones *et al.*, 1993, *J. Virol. Methods* 41:277-96 (cited in the Office Action mailed January 22, 2004), which sought to compare the relative sensitivities and specificities of genomic and oligonucleotide probes, provides further evidence regarding the fundamental differences between oligonucleotide and genomic probes. Because the *oligonucleotide* cocktail disclosed by Meijer *et al.* simply does not comprise *genomic* probes as understood in the art, the reagent recited in claim 1 does not encompass the oligonucleotide cocktail disclosed by Meijer *et al.*

Nevertheless, in order to more particularly point out and distinctly claim the subject matter that Applicants regard as the invention, and in Applicants' view because it will have no substantive effect on the proper scope of the pending claims, Applicants have amended claim 1 so that it is directed to a regent comprising a plurality of genomic HPV DNA probes sets, wherein the individual genomic probe sets comprise a plurality of nucleic acid fragments that detectably hybridize to essentially the full-length genomic sequence of HPV types 16, 18, 31, 33, 35, or 51. Applicants contend that because the oligonucleotide cocktail of Meijer *et al.* does not comprise *genomic* probes, and because the type-specific oligonucleotide probes of reagent disclosed by Meijer *et al.* would not detectably hybridize to essentially the full-length genomic sequence of any one HPV type, Meijer *et al.* cannot anticipate claims 1 and 17. Withdrawal of this rejection is therefore respectfully solicited.

2. Rejections of claims 3 and 19 under 35 U.S.C. § 103

a. Rejection of claims 3 and 19 as being unpatentable over Meijer *et al.* in view of Orth *et al.*

The Office Action asserts a rejection of claims 3 and 19 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of U.S. Patent

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No. 5,981,173 (Orth *et al.*). The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a mixture of probes that is specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58, but not specific for a variety of low-risk HPV types. The Action also states that because there would be more than one copy of each of the individual oligonucleotide probes in the reagent disclosed by Meijer *et al.*, the copies of each oligonucleotide probe comprise "a plurality of nucleic acid fragments." The Action also states that the copies of each oligonucleotide probe are "fragments of the full-length genomic sequence." The Action therefore concludes that the reagent disclosed by Meijer *et al.* is considered to include a plurality of genomic HPV DNA probes sets, wherein the individual genomic probe sets comprise a plurality of nucleic acid fragments of essentially the full-length genomic sequence of HPV types 16, 18, 31, 33, 35, or 51. The Action also states that the probe cocktail disclosed by Meijer *et al.* would have inherently been in a container.

The Action further states that Meijer *et al.* do not disclose a reagent that hybridizes to HPV types 68 and 70, but that Orth *et al.* disclose the genomes of HPV types 68 and 70 and oligonucleotide probes for the detection of HPV types 68 and 70. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included probes specific for HPV types 68 and 70 in the reagent disclosed by Meijer *et al.*, and that one of ordinary skill in the art would have been motivated to do so by the guidance provided in Meijer *et al.* to include additional HPV probes corresponding to newly identified high-risk types as such types are identified.

Applicants respectfully disagree with the Action's assertion that Meijer *et al.* in view of Orth *et al.* results in a *prima facie* case of obviousness with respect to claims 3 and 19. While Meijer *et al.* disclose *oligonucleotide* probes of only 30 nucleotides for HPV genotyping of the amplification product, and Orth *et al.* disclose *oligonucleotide* probes for the detection of HPV types 68 and 70, the reagent of claim 3 (which depends from claim 1), comprises "a plurality of *genomic* HPV DNA probes sets" (*emphasis added*). In addition, the instant specification teaches that the reagent of the invention comprises genomic HPV DNA probes that "are *not* similar to oligonucleotide probes as used in the prior art" (page 5, paragraph 1) (*emphasis added*). Moreover, the difference between the

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genomic probes recited in claim 3 and the oligonucleotide probes disclosed by Meijer *et al.* is well understood in the art. Specifically, one of ordinary skill in the art would understand that the oligonucleotide probes disclosed by Meijer *et al.* correspond to a small portion of the entire HCV genome (about 0.38%), while genomic probes comprise a plurality of nucleic acid fragments that detectably hybridize to essentially the full-length genomic sequence. In addition, Faulkner-Jones *et al.*, 1993, *J. Virol. Methods* 41:277-96 (cited in the Office Action mailed January 22, 2004), which sought to compare the relative sensitivities and specificities of genomic and oligonucleotide probes, provides further evidence regarding the fundamental differences between oligonucleotide and genomic probes. Because an oligonucleotide cocktail comprising the *oligonucleotide* probes disclosed by Meijer *et al.* and Orth *et al.* simply does not comprise *genomic* probes as understood in the art, Meijer *et al.* in view of Orth *et al.* does not result in a *prima facie* case of obviousness with respect to claims 3 and 19.

Nevertheless, as discussed in section 1 above, in order to more particularly point out and distinctly claim the subject matter that Applicants regard as the invention, and in Applicants' view because it will have no substantive effect on the proper scope of the pending claims, Applicants have amended claim 1 so that it is directed to a regent comprising a plurality of genomic HPV DNA probes sets, wherein the individual genomic probe sets comprise a plurality of nucleic acid fragments that detectably hybridize to essentially the full-length genomic sequence of HPV types 16, 18, 31, 33, 35, or 51. Applicants contend that because an oligonucleotide cocktail comprising the *oligonucleotide* probes disclosed by Meijer *et al.* and Orth *et al.* does not comprise *genomic* probes, and because the type-specific oligonucleotide probes of such a cocktail would not detectably hybridize to essentially the full-length genomic sequence of any one HPV type, Meijer *et al.* in view of Orth *et al.* does not result in a *prima facie* case of obviousness with respect to claims 3 and 19. Withdrawal of this rejection is therefore respectfully solicited.

b. Rejection of claims 7 and 22 as being unpatentable over Meijer *et al.* in view of Bauer *et al.*

The Office Action also asserts a rejection of claims 7 and 22 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of U.S.

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Patent No. 5,639,871 (Bauer *et al.*). The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a mixture of probes that is specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58, but not specific for a variety of low-risk HPV types. The Action also states that because there would be more than one copy of each of the individual oligonucleotide probes in the reagent disclosed by Meijer *et al.*, the copies of each oligonucleotide probe comprise "a plurality of nucleic acid fragments." The Action also states that the copies of each oligonucleotide probe are "fragments of the full-length genomic sequence." The Action therefore concludes that the reagent disclosed by Meijer *et al.* is considered to include a plurality of genomic HPV DNA probes sets, wherein the individual genomic probe sets comprise a plurality of nucleic acid fragments of essentially the full-length genomic sequence of HPV types 16, 18, 31, 33, 35, or 51.

The Action also states that the probe cocktail disclosed by Meijer *et al.* would have inherently been in a container. The Action further states that Meijer *et al.* do not disclose a reagent comprising probes that are present in the proportions recited in claim 7, but that the optimization of hybridization assays by determining ideal probe concentrations was routine in the prior art at the time the invention was made (as exemplified by Bauer *et al.*). The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have experimented with different probe concentrations so as to arrive at an optimal concentration for the detection of HPV in a sample.

Applicants respectfully disagree with the Action's assertion that Meijer *et al.* in view of Bauer *et al.* results in a *prima facie* case of obviousness with respect to claims 7 and 22. While Meijer *et al.* disclose *oligonucleotide* probes of only 30 nucleotides for HPV genotyping of the amplification product, the reagent of claim 7 (which depends from claim 1), comprises "a plurality of *genomic* HPV DNA probes sets" (*emphasis added*). In addition, the instant specification teaches that the reagent of the invention comprises genomic HPV DNA probes that "are *not* similar to oligonucleotide probes as used in the prior art" (page 5, paragraph 1) (*emphasis added*). Moreover, the difference between the genomic probes recited in claim 7 and the oligonucleotide probes disclosed by Meijer *et al.* is well understood in the art. Specifically, one of ordinary skill in the art

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would understand that the oligonucleotide probes disclosed by Meijer *et al.* correspond to a small portion of the entire HCV genome (about 0.38%), while genomic probes comprise a plurality of nucleic acid fragments that detectably hybridize to essentially the full-length genomic sequence. In addition, Faulkner-Jones *et al.*, 1993, *J. Virol. Methods* 41:277-96 (cited in the Office Action mailed January 22, 2004), which sought to compare the relative sensitivities and specificities of genomic and oligonucleotide probes, provides further evidence regarding the fundamental differences between oligonucleotide and genomic probes. Because an oligonucleotide cocktail comprising *oligonucleotide* probes simply does not comprise *genomic* probes as understood in the art, Meijer *et al.* in view of Bauer *et al.* does not result in a *prima facie* case of obviousness with respect to claims 7 and 22.

Nevertheless, as discussed in section 1 above, in order to more particularly point out and distinctly claim the subject matter that Applicants regard as the invention, and in Applicants' view because it will have no substantive effect on the proper scope of the pending claims, Applicants have amended claim 1 so that it is directed to a regent comprising a plurality of genomic HPV DNA probes sets, wherein the individual genomic probe sets comprise a plurality of nucleic acid fragments that detectably hybridize to essentially the full-length genomic sequence of HPV types 16, 18, 31, 33, 35, or 51. Applicants contend that because an oligonucleotide cocktail comprising *oligonucleotide* probes does not comprise *genomic* probes, and because the type-specific oligonucleotide probes of such a cocktail would not detectably hybridize to essentially the full-length genomic sequence of any one HPV type, Meijer *et al.* in view of Bauer *et al.* does not result in a *prima facie* case of obviousness with respect to claims 7 and 22. Withdrawal of this rejection is therefore respectfully solicited.

c. Rejection of claims 1, 3, 17, and 19 as being unpatentable over Nuovo *et al.* in view of Cox *et al.*

The Office Action asserts a rejection of claims 1, 3, 17, and 19 under 35 U.S.C. § 103(a), as being unpatentable over Nuovo *et al.*, 1995, *J. Histotechnology* 18:105-110 in view of Cox *et al.*, 1995, *Am. J. Obstet. Gynecol.* 172:946-54. The Action states that Nuovo *et al.* disclose "a reagent for detecting human papilloma virus DNA in a cell sample comprising a plurality of genomic DNA

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probe sets, wherein each probe set comprises a plurality of nucleic acid fragments of essentially the full-length genomic sequence of HPV type 16 that detectably hybridize to substantially all of the full-length genomic sequence of HPV types 16 and 18, as well as 31, 33, and 35" (p. 6). The Action also states that Nuovo *et al.* disclose "probe mixes provided by Digene [Diagnostics] that are made using the entire genome and that contain probes for these groups of HPV subtypes" (*id.*). The Action further states that "the cross-hybridization of the probes taught by Nuovo *et al.* to the genomic sequences of HPV types 39, 45, 52, 56, 58, 59, 68, and 70 is a necessary property of the probes taught by Nuovo *et al.*" (p. 6-7), as evidenced by the instant specification which teaches that a genomic probe set derived from HPV type 18 hybridizes to HPV types 18, 39, 45, 56, 59, 68, and 70, and a genomic probe set derived from HPV type 33 hybridizes to HPV types 16, 31, 33, 35, 45, 52, and 58. The Action also states that the probes in the kits provided by Digene Diagnostics would have inherently been in containers.

The Action further states that Nuovo *et al.* do not disclose a reagent comprising genomic probe sets that are fragments of essentially the full-length genomic sequence of all of the HPV types listed in claim 1, but that Cox *et al.* disclose a single reagent comprising RNA probes to a group of high-risk types including HPV types 16, 18, 31, 33, 35, 45, 51, 52, and 56, and further, that Cox *et al.* suggest adding RNA probes for HPV types 39 and 58 to this reagent. The Action also states that because cross-hybridization of the reagent disclosed by Nuovo *et al.* in view of Cox *et al.* with low-risk HPV types would not be expected at very high stringency conditions, it would be a necessary property of the probe set taught by Nuovo *et al.* in view of Cox *et al.* that it not detectably hybridize to the genomic sequence of a low-risk HPV type. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the reagent disclosed by Nuovo *et al.* to include additional probes from the reagent disclosed by Cox *et al.*, and that one of ordinary skill in the art would have been motivated to do so in order to provide a DNA probe cocktail having the ability to detect as many different HPV types as the reagent disclosed by Cox *et al.*, but that would be more stable in solution than the RNA probe cocktail disclosed by Cox *et al.*

Applicants note that an analysis of obviousness must be based on the following factual inquiries: (1) the scope and content of the prior art; (2) the differences between the prior art and the

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claims at issue; (3) the level of ordinary skill in the art at the time the invention was made; and (4) objective evidence of nonobviosuness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). Moreover, where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 *also requires* consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). As the Federal Circuit has emphasized: "[b]oth the suggestion and the reasonable expectation of success must be founded in the prior art, not the Applicants' disclosure." *Id.*

Applicants respectfully disagree with the Action's assertion that Nuovo *et al.* in view of Cox *et al.* results in a *prima facie* case of obviousness with respect to claims 1, 3, 17, and 19. In particular, Applicants disagree with the Action's characterization of the Nuovo *et al.* reference, and with the Action's use of improper hindsight reasoning to combine the Nuovo *et al.* and Cox *et al.* references. Nuovo *et al.* describes the use of eight different HPV probe kits, four of which were obtained from Digene Diagnostics (Silver Spring, MD) and four of which were obtained from ONCOR (Gaithersburg, MD) (page 106). Both Digene Diagnostics and ONCOR provided HPV probe kits – referred to as Omniprobe and the wide spectrum probe cocktail, respectively – that were capable of detectably hybridizing to the sequence of HPV types 6, 11, 16, 18, 31, 33, 35, 42, 43, 44, 45, and 51 (*id.*). Since each of these probe kits was capable of detectably hybridizing to the sequence of low-risk HPV types 6 and 11, both of these kits would detectably hybridize to the genomic sequence of a low-risk HPV type. Because the prior art references being combined must teach or suggest all of a claim's limitations (M.P.E.P. § 2142), neither the use of Digene Diagnostics' Omniprobe nor the use of ONCOR's wide spectrum probe cocktail can be used to establish a *prima facie* case of obviousness with respect to claims 1, 3, 17, and 19.

Nuovo *et al.* also describe the use of probe kits for specific HPV types (page 106). Specifically, Nuovo *et al.* describe the use of three *separate* probe kits, obtained from both Digene Diagnostics and ONCOR, which contain probes for *either* (1) HPV types 6 and 11; (2) HPV types 16 and 18; or (3) HPV types 31, 33, and 35 (*id.*). Since the probe kits obtained from ONCOR were

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generated from specific subgenomic areas in order to minimize crosshomology with other known HPV types (*id.*), the ONCOR probe mixes neither comprise a plurality of *genomic* HPV probe sets or detectably hybridize to essentially the full-length genomic sequence of HPV (in addition, the probe kit for HPV types 6 and 11 would detectably hybridize to the genomic sequence of a low-risk HPV type). Because the prior art references being combined must teach or suggest all of a claim's limitations (M.P.E.P. § 2142), the use of ONCOR's type-specific probe kits cannot be used to establish a *prima facie* case of obviousness with respect to claims 1, 3, 17, and 19.

With regard to Digene Diagnostics' type-specific probe kits, the probe kit for HPV types 6 and 11 would detectably hybridize to the genomic sequence of a low-risk HPV type, the probe kit for HPV types 16 and 18 would not *detectably* hybridize to essentially the full-length genomic sequence of HPV types 33, 35, and 51 as required by independent claim 1, and the probe kit for HPV types 31, 33, and 35 would not *detectably* hybridize to essentially the full-length genomic sequence of HPV type 18 as required by independent claim 1. Moreover, Nuovo *et al.* would have recognized that the probe sets for HPV types 16/18 and 31/33/35 were each incapable of detectably hybridizing to essentially the full-length genomic sequence of the HPV types recited in independent claim 1 *only* by considering Applicants' teachings (specifically, the teachings on pages 8-9 of Applicants' specification). Because the teaching or suggestion to make the claimed combination must be found in the prior art, and not in Applicants' disclosure (*In re Vaeck*, 947 F.2d at 493; M.P.E.P. § 2143.01), the use of Digene Diagnostics' type-specific probe kits cannot be used to establish a *prima facie* case of obviousness with respect to claims 1, 3, 17, and 19.

Applicants next address the specific assertions made in the pending Action with regard to the Nuovo *et al.* disclosure. First, with regard to the assertion that Nuovo *et al.* disclose "a reagent . . . comprising a plurality of genomic DNA probe sets, wherein each probe set comprises a plurality of nucleic acid fragments of essentially the full-length genomic sequence of HPV type 16 that detectably hybridize to substantially all of the full-length genomic sequence of HPV types 16 and 18, as well as 31, 33, and 35" (p. 6), Applicants contend that the explicit teachings of the specification contradict such a conclusion. As discussed above, even a type-specific probe set for *both* HPV types 16 and 18 would not *detectably* hybridize to essentially the full-length genomic sequence of HPV types 33, 35, and 51, let alone a "probe set compris[ing] a plurality of nucleic acid fragments of

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essentially the full-length genomic sequence of HPV type 16." Moreover, Applicants are confused by the Action's continued use of the phrase "detectably hybridize to *substantially all* of the full-length genomic sequence" (*emphasis added*), since Applicants amended claims 1 and 3 in their response to the Office Action mailed October 20, 2004 to delete the phrase "substantially all." Next, with regard to the assertion that Nuovo *et al.* disclose "probe mixes provided . . . made using the entire genome and that contain probes for these groups of HPV subtypes" (p. 6), Applicants do not understand what the Action means by the phrase "these groups of HPV subtypes." If the Action is asserting that Nuovo *et al.* used a probe kit containing probes derived from the entire genome of *only* HPV types 16, 18, 31, 33, and 35, however, this is simply not the case. As discussed above, four of the eight probe kits used by Nuovo *et al.* contained probes for low-risk HPV types 6 and 11, and the remaining four probe kits contained probes for *either* HPV types 16 and 18 or HPV types 31, 33, and 35. Finally, Applicants contend that the assertion that "the cross-hybridization of the probes taught by Nuovo *et al.* to the genomic sequences of HPV types 39, 45, 52, 56, 58, 59, 68, and 70 is a necessary property of the probes taught by Nuovo *et al.*" (p. 6-7) mischaracterizes the actual teachings of Nuovo *et al.* Even if it were clear that Digene Diagnostics' Omniprobe was capable of detectably hybridizing to the sequence of HPV types 39, 45, 52, 56, 58, 59, 68, and 70 – which it is not, since Nuovo *et al.* does not disclose the exact composition of this probe – it is clear that this probe would detectably hybridize to the genomic sequence of a low-risk HPV type (*i.e.*, HPV types 6 and 11).

Applicants contend that the disclosure of Cox *et al.* does not cure the deficiencies and limited disclosure of Nuovo *et al.* because the Action uses improper hindsight reasoning to combine these references. The Action asserts that one of ordinary skill in the art, in view of the Nuovo *et al.* and Cox *et al.* disclosures, would know to make a reagent comprising a plurality of genomic HPV DNA probe sets, wherein the genomic HPV DNA probe set comprises a plurality of nucleic acid fragments that detectably hybridize to essentially the full-length genomic sequence of HPV types 16, 18, 31, 33, 35, and 51, and wherein the genomic HPV DNA probe sets do not detectably hybridize to the genomic sequence of a low-risk HPV type. The Action's argument appears to be based on the disclosure in Nuovo *et al.* of two reagents comprising genomic HPV DNA probe sets for HPV types 16 and 18 and for HPV types 31, 33, and 35 (p. 106); the disclosure in Cox *et al.* of a hybrid capture

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method using a reagent comprising RNA probes for HPV types 16, 18, 31, 33, 35, 45, 51, and 52 (p. 948); and the knowledge of one of ordinary skill in the art that genomic HPV DNA probes would be more stable in solution than RNA probes.

Applicants contend that the reasoning set forth in the Action is improper and clearly contravenes the Federal Circuit's requirement that the teaching or suggestion to make the claimed combination must be found in the prior art (*In re Vaeck*, 947 F.2d at 493; M.P.E.P. § 2143.01). Applicants also contend that absent Applicants' teachings, neither Nuovo *et al.* nor Cox *et al.* would have appreciated the benefits of using a reagent comprising *genomic* DNA probes; namely, that a reagent comprising only six high-risk genomic HPV DNA probe sets would allow for the detection of at least thirteen high-risk HPV types without cross-reacting with low-risk HPV types. Furthermore, Applicants contend that one of ordinary skill in the art would not know to substitute the *RNA* probes of the hybrid capture method disclosed by Cox *et al.* with *genomic DNA* probes because the latter would simply not work. In the hybrid capture method disclosed by Cox *et al.*, single-stranded DNA isolated from a cell sample is allowed to hybridize to RNA probes corresponding to a number of high-risk HPV types, and RNA/DNA hybrids that form are immobilized in a capture tube coated with antibodies *specific for RNA/DNA hybrids* (p. 948). Since the use of a reagent comprising *RNA probes* is a necessary requirement of the method disclosed by Cox *et al.*, one of ordinary skill would not, as the Action suggests, substitute the RNA probes of this method with genomic DNA probes. The relative stability of RNA and genomic DNA probes would simply not be a relevant consideration.

Applicants contend that for the reasons listed above, Nuovo *et al.* in view of Cox *et al.* does not result in a *prima facie* case of obviousness with respect to claims 1, 3, 17, and 19. Withdrawal of this rejection is therefore respectfully solicited.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Switzer believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

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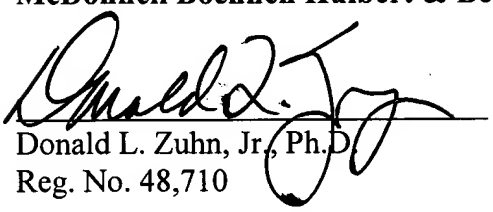
Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff

Dated: July 5, 2005

By: 
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